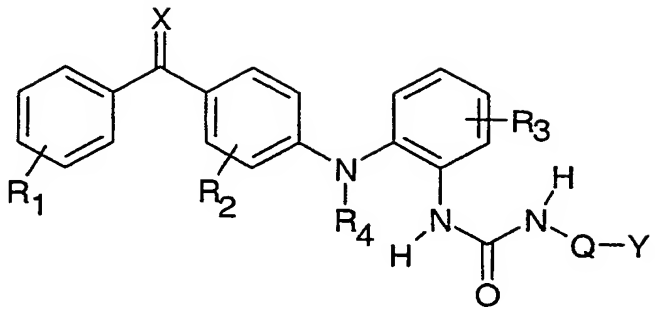
CLAIMS

1. A compound of the formula I



I

wherein R_1 independently represents one or more, same or different substituents selected from the group consisting of halogen, hydroxy, mercapto, trifluoromethyl, amino, (C_1-C_3)alkyl, (C_2-C_3)olefinic group, (C_1-C_3)alkoxy, (C_1-C_3)alkylthio, (C_1-C_6)alkylamino, (C_1-C_3)alkoxycarbonyl, cyano, carbamoyl, phenyl and nitro, provided that when R_1 represents one substituent, it is in the ortho position, and when R_1 represents more than one substituent, at least one R_1 substituent is in the ortho position; R_2 is one substituent in the ortho position, said substituent being selected from the group consisting of hydrogen, halogen, hydroxy, mercapto, trifluoromethyl, amino, (C_1-C_3)alkyl, (C_2-C_3)olefinic group, (C_1-C_3)alkoxy, (C_1-C_3)alkylthio, (C_1-C_6)alkylamino, (C_1-C_3)alkoxycarbonyl, cyano, carbamoyl, phenyl and nitro;

R_3 represents hydrogen, halogen, hydroxy, mercapto, trifluoromethyl, amino, (C_1-C_3)alkyl, (C_2-C_3)olefinic group, (C_1-C_3)alkoxy, (C_1-C_3)alkylthio, (C_1-C_6)alkylamino, (C_1-C_3)alkoxycarbonyl, phenyl, cyano, carboxy, or carbamoyl;

R_4 represents hydrogen, (C_1-C_3)alkyl, or allyl;

Q represents a bond, $-SO_2-$, or $-C(R_6)(R_7)(-O-C=O)-$, in which formula R_6 and R_7 independently represent hydrogen, trifluoromethyl, or (C_1-C_4)alkyl;

Y represents (C_1-C_{15})alkyl, (C_2-C_{15})olefinic group, (C_3-C_{10})carbocyclic group, or phenyl, any of which is optionally substituted by one or more, same or different substituents represented by the formula R_5; or Y represents a group of

formula -(Z-O)$_n$-Z, where Z is a (C_1-C_3)alkyl and n is an integer > 1, and no continuous linear sequence of atoms in the group Y exceeds 15;

R_5 represents halogen, hydroxy, mercapto, trifluoromethyl, (C_1-C_4)alkyl, amino, (C_1-C_3)alkoxy, (C_1-C_3)alkylthio, (C_1-C_6)alkylamino, (C_1-C_3)alkoxycarbonyl, cyano, azido, nitro, -COOH, -$CONH_2$, -CONHR', or -CONRR' wherein R and R' stands for (C_1-C_3)alkyl;

X represents oxygen or sulphur,

or a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

2. A compound according to claim 1 wherein independently

- R_1 represents one or more, same or different substituents selected from the group consisting of fluoro, chloro, bromo, hydroxy, trifluoromethyl, amino, (C_1-C_2)alkyl, (C_2-C_3)alkenyl, (C_1-C_3)alkoxy, (C_1-C_3)alkoxycarbonyl, or cyano.

- R_2 represents one or more, same or different substituents selected from the group consisting of hydrogen, fluoro, chloro, bromo, hydroxy, trifluoromethyl, amino, (C_1-C_2)alkyl, (C_2-C_3)alkenyl, (C_1-C_3)alkoxy.

- R_3 represents one or more, same or different substituents selected from the group consisting of hydrogen, fluoro, chloro, bromo, hydroxy, trifluoromethyl, (C_1-C_3)alkyl, (C_2-C_3)alkenyl, (C_1-C_3)alkoxy, (C_1-C_3)alkoxycarbonyl, cyano, or carboxy.

- R_4 represents hydrogen, (C_1-C_2)alkyl, or allyl.

- X represents oxygen.

- Q represents a bond or -SO_2-.

- Y represents (C_1-C_6)alkyl; (C_2-C_6)alkenyl; (C_3-C_6)cycloalkyl; (C_5-C_8)cycloalkene group; or phenyl; any of which is optionally substituted by one or more, same or different substituents selected from the group consisting of the formula R_5, R_5 representing fluoro, chloro, bromo, hydroxy, amino, (C_1-C_2)alkoxy, (C_1-C_4)alkylamino, (C_1-C_3)alkoxycarbonyl, cyano, azido, -COOH, $-CONH_2$, -CONHR', or -CONR'R' wherein R' represents (C_1-C_2)alkyl.

Sub A2

3. A compound according to any one of the preceding claims wherein R_1 represents one or more, same or different substituents selected from the group consisting of fluoro, chloro, bromo, hydroxy, methyl, or methoxy.

4. A compound according to any one of the preceding claims wherein R_1 is methyl and R_2 is Cl.

5. A compound according to claim 1 selected from the group consisting of
1-Cyclohexyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 101),
1-Ethyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 102),
1-[2-[3-Chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]-3-phenylurea (Compound 103),
1-Butyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 104),
1-[2-[3-Chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]-3-*iso*-propylurea (Compound 108),
1-[2-[3-Chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]-3-propylurea (Compound 109),
1-Methyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 110),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(2-methylbenzoyl)-phenylamino] phenyl]urea (Compound 112),
1-Ethyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]-5-fluoro-phenyl]urea (Compound 114),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(2,5-dimethylbenzoyl)-phenylamino]phenyl]urea (Compound 117),

1-Ethyl-3-[5-bromo-2-[3-chloro-4-(4-chloro-2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 121),
1-Ethyl-3-[5-bromo-2-[3-fluoro-4-(4-methoxy-2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 123),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(2,4,5-trimethylbenzoyl)-phenylamino]phenyl]urea (Compound 124),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(4-fluoro-2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 125),
1-Ethyl-3-[5-bromo-2-[3-fluoro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 126),
and salts thereof with pharmaceutically acceptable acids, hydrates and solvates.

Sub A31

6. A pharmaceutical composition containing as an active ingredient a compound according to any one of claims 1 to 5 together with a pharmaceutically acceptable carrier and optionally together with a second active ingredient optionally selected from the group consisting of glucocorticoids, vitamin D's, anti-histamines, platelet activating factor (PAF) antagonists, anticolinergic agents, methyl xanthines, β-adrenergic agents, salicylates, indomethacin, flufenamate, naproxen, timegadine, gold salts, penicillamine, serum cholesterol-reducing agents, retinoids, zinc salts, and salicylazosulfapyridin (Salazopyrin).

7. Use of a compound according to any one of claim 1 to 5 for the preparation of a medicament for the treatment and/or prophylaxis of asthma, allergy, arthritis, including rheumatoid arthritis and spondyloarthritis, gout, atherosclerosis, chronic inflammatory bowel disease (Crohn's disease), proliferative and inflammatory skin disorders, such as psoriasis, atopic dermatitis, uveitis, septic shock, AIDS, osteoporosis and acne.

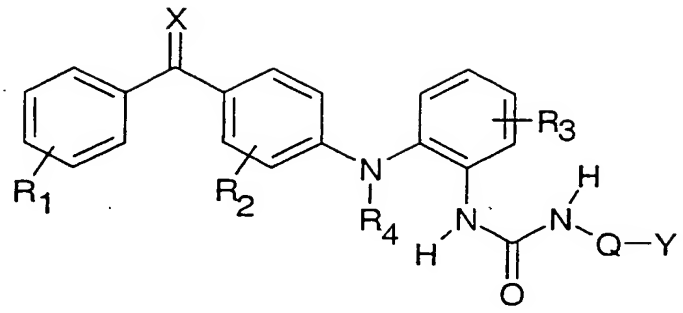
8. A method for the treatment and/or prophylaxis of asthma, allergy, arthritis, including rheumatoid arthritis and spondyloarthritis, gout, atherosclerosis, chronic inflammatory bowel disease (Crohn's disease), proliferative and inflammatory skin disorders, such as psoriasis, atopic dermatitis, uveitis, septic shock, AIDS, osteoporosis and acne, characterised in administering to a patient suffering from at least one of said diseases an effective amount of one or more compounds according to any one of claims 1 to 5 as an active ingredient alone, or if necessary together with a pharmaceutically acceptable carrier, and, optionally, a second active ingredient optionally selected from the

group consisting of glucocorticoids, vitamin D's, anti-histamines, platelet activating factor (PAF) antagonists, anticolinergic agents, methyl xanthines, β-adrenergic agents, salicylates, indomethacin, flufenamate, naproxen, timegadine, gold salts, penicillamine, serum cholesterol-reducing agents, retinoids, zinc salts, and salicylazosulfapyridin (Salazopyrin).

9. A method of treatment according to the preceding claim comprising administering to a mammal in need of systemic treatment a suitable dose of a compound of formula I of from 0.1 to 200 mg/kg bodyweight, preferably a dose of from 0.2 to 50 mg/kg of mammal bodyweight one or more times daily.

CLAIMS

1. A compound of the formula I



I

wherein R_1 and R_2 independently represent one or more, same or different substituents selected from the group consisting of halogen, hydroxy, mercapto, trifluoromethyl, amino, (C_1-C_3)alkyl, (C_2-C_3)olefinic group, (C_1-C_3)alkoxy, (C_1-C_3)alkylthio, (C_1-C_6)alkylamino, (C_1-C_3)alkoxycarbonyl, cyano, carbamoyl, phenyl, and nitro; R_2 further being represented by hydrogen;

R_3 represents hydrogen, halogen, hydroxy, mercapto, trifluoromethyl, amino, (C_1-C_3)alkyl, (C_2-C_3)olefinic group, (C_1-C_3)alkoxy, (C_1-C_3)alkylthio, (C_1-C_6)alkylamino, (C_1-C_3)alkoxycarbonyl, phenyl, cyano, carboxy, or carbamoyl;

R_4 represents hydrogen, (C_1-C_3)alkyl, or allyl;

Q represents a bond, -SO_2-, or -$C(R_6)(R_7)$(-O-C=O)-, in which formula R_6 and R_7 independently represent hydrogen, trifluoromethyl, or (C_1-C_4)alkyl;

Y represents (C_1-C_{15})alkyl, (C_2-C_{15})olefinic group, (C_3-C_{10})carbocyclic group, or phenyl, any of which is optionally substituted by one or more, same or different substituents represented by the formula R_5; or Y represents a group of formula -$(Z\text{-}O)_n$-Z, where Z is a (C_1-C_3)alkyl and n is an integer > 1, and no continuous linear sequence of atoms in the group Y exceeds 15;

R_5 represents halogen, hydroxy, mercapto, trifluoromethyl, (C_1-C_4)alkyl, amino, (C_1-C_3)alkoxy, (C_1-C_3)alkylthio, (C_1-C_6)alkylamino, (C_1-C_3)alkoxycarbonyl, cyano, azido, nitro, -COOH, -$CONH_2$, -CONHR', or -CONRR' wherein R and R' stands for (C_1-C_3)alkyl;

X represents oxygen or sulphur,

or a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

2. A compound according to claim 1 wherein independently

- R_1 represents one or more, same or different substituents selected from the group consisting of fluoro, chloro, bromo, hydroxy, trifluoromethyl, amino, (C_1-C_2)alkyl, (C_2-C_3)alkenyl, (C_1-C_3)alkoxy, (C_1-C_3)alkoxycarbonyl, or cyano.

- R_2 represents one or more, same or different substituents selected from the group consisting of hydrogen, fluoro, chloro, bromo, hydroxy, trifluoromethyl, amino, (C_1-C_2)alkyl, (C_2-C_3)alkenyl, (C_1-C_3)alkoxy.

- R_3 represents one or more, same or different substituents selected from the group consisting of hydrogen, fluoro, chloro, bromo, hydroxy, trifluoromethyl, (C_1-C_3)alkyl, (C_2-C_3)alkenyl, (C_1-C_3)alkoxy, (C_1-C_3)alkoxycarbonyl, cyano, or carboxy.

- R_4 represents hydrogen, (C_1-C_2)alkyl, or allyl.

- X represents oxygen.

- Q represents a bond or $-SO_2-$.

- Y represents (C_1-C_6)alkyl; (C_2-C_6)alkenyl; (C_3-C_6)cycloalkyl; (C_5-C_8)cycloalkene group; or phenyl; any of which is optionally substituted by one or more, same or different substituents selected from the group consisting of the formula R_5, R_5 representing fluoro, chloro, bromo, hydroxy, amino, (C_1-C_2)alkoxy, (C_1-C_4)alkylamino, (C_1-C_3)alkoxycarbonyl, cyano, azido, -COOH, $-CONH_2$, -CONHR', or -CONR'R' wherein R' represents (C_1-C_2)alkyl.

3. A compound according to any one of the preceding claims wherein R_1 represents one or more, same or different substituents selected from the group consisting of fluoro, chloro,

bromo, hydroxy, methyl, or methoxy.

4. A compound according to any one of the preceding claims wherein one or both of R_1 and R_2 represent one substituent, said substituent preferably being in the ortho position.

5. A compound according to any one of the preceding claims wherein R_1 is methyl and R_2 is Cl.

6. A compound according to claim 1 selected from the group consisting of
1-Cyclohexyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 101),
1-Ethyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 102),
1-[2-[3-Chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]-3-phenylurea (Compound 103),
1-Butyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 104),
1-[2-[3-Chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]-3-*iso*-propylurea (Compound 108),
1-[2-[3-Chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]-3-propylurea (Compound 109),
1-Methyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 110),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 112),
1-Ethyl-3-[2-[3-chloro-4-(2-methylbenzoyl)-phenylamino]-5-fluoro-phenyl]urea (Compound 114),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(2,5-dimethylbenzoyl)-phenylamino]phenyl]urea (Compound 117),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(4-chloro-2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 121),
1-Ethyl-3-[5-bromo-2-[3-fluoro-4-(4-methoxy-2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 123),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(2,4,5-trimethylbenzoyl)-phenylamino]phenyl]urea (Compound 124),
1-Ethyl-3-[5-bromo-2-[3-chloro-4-(4-fluoro-2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 125),
1-Ethyl-3-[5-bromo-2-[3-fluoro-4-(2-methylbenzoyl)-phenylamino]phenyl]urea (Compound 126),
and salts thereof with pharmaceutically acceptable acids, hydrates and solvates.

7. A pharmaceutical composition containing as an active ingredient a compound according to any one of claims 1 to 6 together with a pharmaceutically acceptable carrier and optionally together with a second active ingredient optionally selected from the group consisting of glucocorticoids, vitamin D's, anti-histamines, platelet activating factor (PAF) antagonists, anticolinergic agents, methyl xanthines, β-adrenergic agents, salicylates, indomethacin, flufenamate, naproxen, timegadine, gold salts, penicillamine, serum cholesterol-reducing agents, retinoids, zinc salts, and salicylazosulfapyridin (Salazopyrin).

8. Use of a compound according to any one of claim 1 to 7 for the preparation of a medicament for the treatment and/or prophylaxis of asthma, allergy, arthritis, including rheumatoid arthritis and spondyloarthritis, gout, atherosclerosis, chronic inflammatory bowel disease (Crohn's disease), proliferative and inflammatory skin disorders, such as psoriasis, atopic dermatitis, uveitis, septic shock, AIDS, osteoporosis and acne.

9. A method for the treatment and/or prophylaxis of asthma, allergy, arthritis, including rheumatoid arthritis and spondyloarthritis, gout, atherosclerosis, chronic inflammatory bowel disease (Crohn's disease), proliferative and inflammatory skin disorders, such as psoriasis, atopic dermatitis, uveitis, septic shock, AIDS, osteoporosis and acne, characterised in administering to a patient suffering from at least one of said diseases an effective amount of one or more compounds according to any one of claims 1 to 7 as an active ingredient alone, or if necessary together with a pharmaceutically acceptable carrier, and, optionally, a second active ingredient optionally selected from the group consisting of glucocorticoids, vitamin D's, anti-histamines, platelet activating factor (PAF) antagonists, anticolinergic agents, methyl xanthines, β-adrenergic agents, salicylates, indomethacin, flufenamate, naproxen, timegadine, gold salts, penicillamine, serum cholesterol-reducing agents, retinoids, zinc salts, and salicylazosulfapyridin (Salazopyrin).

10. A method of treatment according to the preceding claim comprising administering to a mammal in need of systemic treatment a suitable dose of a compound of formula I of from 0.1 to 200 mg/kg bodyweight, preferably a dose of from 0.2 to 50 mg/kg of mammal bodyweight one or more times daily.